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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,303	10/23/2003	Thomas Primiano	02-1133-C	7346

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,303	PRIMIANO ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-9 are all the pending claims for this application.

Election/Restrictions

2. Applicant's election of Group II (Claims 8 and 9) in the reply filed on May 12, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8 and 9 are the claims under examination. Claims 1-7 are withdrawn as being drawn to non-elected subject matter.

Specification

3. The Abstract of Disclosure is objected to for the following reasons:

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoefnagel et al. (European J. Nuclear Medicine 28:359-368 (March 2001); hereinafter referred to as "Hoefnagel").

Claims 8 and 9 are drawn to a pharmaceutical composition comprising an anti-human L1CAM antibody and a pharmaceutical excipient.

Hoefnagel discloses the therapeutic efficacy of ^{131}I-labeled chCE7 (chimeric murine anti-human L1CAM mAb) in nude mice bearing neuroblastoma xenografts (Materials and Methods). ^{131}I-labeled chCE7 specifically bound to neuroblastoma cell lines and Foehn renal carcinoma cell line (Figure 1). The data in Figure 3 show neuroblastoma growth inhibition in mice i.v. injected with the ^{131}I-labeled chCE7 Mab in saline. Hoefnagel teaches a composition comprising an L1CAM antibody (^{131}I-labeled chCE7 Mab) and an excipient (saline).

Applicant is reminded that because the claims recite "comprising" language, any conjugated or unconjugated human L1CAM antibody with an excipient is thereby encompassed, and thus anticipated by Hoefnagel.

5. Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Carrel et al. (Nuclear Medicine Biol. 24(6):539-546 (August 1997); hereinafter referred to as "Carrel").

The interpretation of Claims 8 and 9 is discussed, supra.

Carrel discloses that radioiodinated chCE7 $F(ab)'_2$ fragments dissolved in buffer or PBS (p. 542, Col. 1, ¶2) retained binding affinity comparable to the parent chCE7 Mab, were heat stable with respect to refolding and could internalize into neuroblastoma tumor cells in vivo. Carrel teaches a composition comprising an L1CAM Mab and an L1CAM-binding fragment (^{131}I-labeled chCE7 Fab) and an excipient (PBS or buffer).

Applicant is reminded that because the claims recite "comprising" language, any conjugated or unconjugated human L1CAM Mab or human L1CAM binding fragment with an excipient are thereby encompassed, and thus anticipated by Carrel.

6. Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mujoo et al. (J. Biol. Chem. 261:10299 –10305 (1986); hereinafter referred to as "Mujoo") as evidenced by Wolff et al (J. Biol. Chem. 263:11943-11947 (1988); hereinafter referred to as "Wolff").

The interpretation of Claims 8 and 9 is discussed supra.

Mujoo discloses that the 5G3 Mab dissolved in 0.5% BSA/PBS binds to human neuroblastoma, melanoma, squamous lung carcinoma, squamous skin carcinoma and osteogenic sarcoma cell lines (Tables 1 and 2), and as evidenced by Wolff (see entire reference), the 5G3 Mab of Mujoo recognizes the human L1 cell adhesion molecule

equivalent of murine L1 antigen. Mujoo discloses "because of the relatively good specificity and surface expression of its target antigen, Mab 5G3 may prove to be an effective device for targeting covalently linked drugs or radionuclides to human neuroblastoma tumors and thereby provide a useful adjunct for the treatment of this cancer (p. 10305, Col. 1, ¶3). Mojoo as evidenced by Wolff teaches a composition comprising an L1CAM antibody (5G3 Mab) and an excipient (0.5% BSA/PBS), thus the claims are anticipated by Mojoo and Wolff.

7. Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. (Hybridoma 10:481-491 (1991); hereinafter referred to as "Patel").

The interpretation of Claims 8 and 9 is discussed supra.

Patel discloses that the human L1CAM Mab, UJ127.11, dissolved in PBS binds to human L1 antigen on neuroblastoma lines and rhabdomyosarcoma cell line JR1, but no binding was noted to hematopoietic cells. Patel discloses that UJ127.11 and 5G3 have very similar binding profiles for human L1 (Table 1). Patel discloses another human L1CAM Mab, UJ181.4, "although the reagent recognizes a different epitope to UJ127.11" (p. 488, ¶5). Patel discloses using the antibody reagents to investigate "involvement of L1 in human neurosurgical diseases and cancer" (p. 482, ¶2; p. 489, ¶2). Patel teaches a composition comprising an L1CAM antibody (UJ127.11, 5G3 or UJ181.4) and an excipient (PBS), thus the claims are anticipated by Patel.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rathjen et al. (EMBO J. 3:1-10 (1984); hereinafter referred to as "Rathjen") in view of Cleland et al. (J. Pharm. Sci. 90:310-321 (2001); hereinafter referred to as "Cleland").

The interpretation of Claim 8 is discussed supra.

Rathjen discloses murine L1 polyclonal and monoclonal antibodies and reactivity with C1300 neuroblastoma clones NB41A3 and N2A (p. 3, Col. 2, ¶2- p. 4, Col. 1, ¶1). Fab fragments of polyclonal antibodies dissolved in culture medium, calcium, magnesium free-HBSS, were shown to inhibit aggregation of the neuroblastoma clone N2A (Table II; Figures 7 and 8). Rathjen does not disclose a pharmaceutical excipient.

Cleland discloses the selection of pharmaceutically acceptable excipients for a recombinant humanized Mab, rhu MAB HER2, in order to preserve protein stability.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced the instant claimed composition in view of Rathjen and Cleland. Rathjen discloses the involvement of L1 in cell adhesion of tumor cell lines using the disclosed antibodies to block this interaction, and Cleland discloses preserving antibody structure with excipients, thus one skilled in the art could have readily produced a composition comprising the antibody of Rathjen and the excipients of Cleland to create a pharmaceutical composition which retains the L1CAM binding property of the L1CAM antibody or antibody binding fragment thereof. Thus, the claim was prima facie obvious at the time of the invention in view of Rathjan and Cleland.

9. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (J. Biol. Chem. 263:11943-11947 (1988); hereinafter referred to as "Wolff") in view of Cleland et al. (J. Pharm. Sci. 90:310-321 (2001); hereinafter referred to as "Cleland").

The interpretation of Claims 8 and 9 is discussed supra.

Wolff discloses that the human 5G3 antigen is the same protein as murine L1 antigen using the 5G3 Mab and rabbit-anti human 5G3 polyclonal antibodies by comparing immunological and biochemical cross-reactivity on a neuroblastoma cell line (Figure 1). Wolff discloses the potential involvement of 5G3 or L1 in various human neurological disorders. Wolff does not disclose using the antibodies in combination with a pharmaceutical excipient.

See the interpretation of Cleland as discussed supra.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced the instant claimed composition in view of Wolff and Cleland. Wolff discloses the involvement of L1 (L1CAM) in human neurological disorders using the disclosed monoclonal and polyclonal antibodies to identify L1 in human neuroblastoma cells, and Cleland discloses preserving antibody structure with excipients, thus one skilled in the art could have readily produced a composition comprising the antibody of Wolff and the excipients of Cleland to create a pharmaceutical composition which retains the L1CAM binding property of the L1CAM antibody or antibody binding fragment thereof. Thus, the claims were prima facie obvious at the time of the invention in view of Wolff and Cleland.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER